BSCL2 gene

BSCL2, seipin lipid droplet biogenesis associated

Normal Function

The *BSCL2* gene provides instructions for making a protein called seipin, whose function is unknown. Within cells, seipin is located in the membrane of a structure called the endoplasmic reticulum. The endoplasmic reticulum modifies newly produced proteins and also helps transport proteins, fats, and other molecules to specific sites either inside or outside the cell.

The *BSCL2* gene is active in cells and tissues throughout the body, particularly in nerve cells that control muscle movement (motor neurons) and in the brain. The gene is also active in fat-storing cells called adipocytes, which are the major component of fatty (adipose) tissue. Studies suggest that seipin plays a critical role in the development and function of adipocytes. In particular, seipin is involved in the development of lipid droplets, which are structures within these cells that store fat molecules.

Health Conditions Related to Genetic Changes

Charcot-Marie-Tooth disease

A *BSCL2* gene mutation has been reported in a small number of people with Charcot-Marie-Tooth disease type 2, a disorder that affects the peripheral nerves. Peripheral nerves connect the brain and spinal cord to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound.

The *BSCL2* gene mutation identified in some individuals with Charcot-Marie-Tooth disease changes one of the protein building blocks (amino acids) in the seipin protein. Specifically, the amino acid asparagine is replaced with the amino acid serine at protein position 88 (written as Asn88Ser or N88S). It is unclear how this mutation causes the disorder. The mutation probably alters the structure of seipin, causing it to fold into an incorrect 3-dimensional shape. Research findings indicate that misfolded seipin proteins build up in the endoplasmic reticulum. This accumulation likely damages and kills motor neurons, which leads to muscle weakness in the arms and legs, a characteristic feature of Charcot-Marie-Tooth disease.

congenital generalized lipodystrophy

At least 24 mutations in the *BSCL2* gene have been identified in people with congenital generalized lipodystrophy (also called Berardinelli-Seip congenital lipodystrophy) type 2. This rare condition is characterized by an almost total absence of adipose tissue and a very muscular appearance. A shortage of adipose tissue

leads to multiple health problems, including high levels of fats called triglycerides circulating in the bloodstream (hypertriglyceridemia) and diabetes mellitus. In some cases, this form of the condition is also associated with intellectual disability, which is usually mild to moderate.

Most of the *BSCL2* gene mutations that cause congenital generalized lipodystrophy type 2 lead to the production of a nonfunctional version of the seipin protein or prevent cells from making any of this protein. A loss of functional seipin disrupts the normal development and function of adipocytes, including lipid droplets, which prevents fats from being stored normally in adipose tissue. The resulting lack of body fat underlies most of the signs and symptoms of congenital generalized lipodystrophy type 2. A loss of seipin function in the brain may help explain why intellectual disability can occur with this form of the condition.

distal hereditary motor neuropathy, type V

At least two *BSCL2* gene mutations have been identified in people with distal hereditary motor neuropathy, type V, a progressive disorder that affects motor neurons in the spinal cord. It results in muscle weakness and affects movement of the hands and feet. The mutations that can cause this disorder each change a single amino acid in the seipin protein. In one mutation, the amino acid serine is replaced with the amino leucine at position 90 (written as Ser90Leu or S90L). The other is the N88S mutation, described above.

It is unclear how *BSCL2* gene mutations cause distal hereditary motor neuropathy, type V. These genetic changes probably alter the structure of seipin, causing it to fold into an incorrect 3-dimensional shape. Research findings indicate that misfolded seipin proteins build up in the endoplasmic reticulum. This accumulation likely damages and kills motor neurons, which leads to muscle weakness.

Silver syndrome

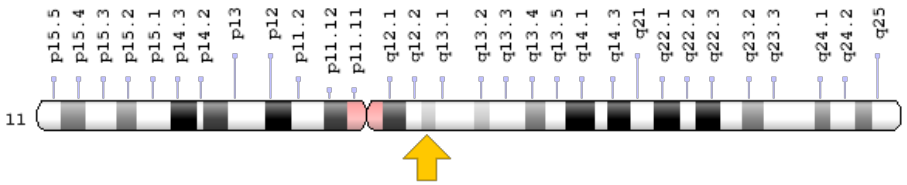
At least two mutations in the *BSCL2* gene, the N88S and S90L mutations described above, have been reported to cause Silver syndrome. This condition is characterized by muscle weakness and wasting in the hands and abnormal muscle stiffness (spasticity) in the legs. The mutations likely result in misfolded seipin proteins that accumulate within neurons, leading to cell damage and cell death. The loss of neurons causes muscle weakness and spasticity in people with Silver syndrome.

It is unclear how the same mutations in the *BSCL2* gene can cause Silver syndrome, Charcot-Marie-Tooth syndrome, or distal hereditary motor neuropathy, type V in different people. People with Silver syndrome sometimes have family members with the same *BSCL2* gene mutation who have one of these other conditions.

Chromosomal Location

Cytogenetic Location: 11q12.3, which is the long (q) arm of chromosome 11 at position 12.3

Molecular Location: base pairs 62,690,262 to 62,709,619 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- Berardinelli-Seip congenital lipodystrophy 2 (seipin)
- BSCL2_HUMAN
- GNG3LG
- seipin
- SPG17

Additional Information & Resources

Educational Resources

- The Cell: A Molecular Approach (second edition, 2000): The Endoplasmic Reticulum
  https://www.ncbi.nlm.nih.gov/books/NBK9889/

GeneReviews

- Berardinelli-Seip Congenital Lipodystrophy
  https://www.ncbi.nlm.nih.gov/books/NBK1212
- BSCL2-Related Neurologic Disorders/Seipinopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1307
- Charcot-Marie-Tooth Neuropathy Type 2
  https://www.ncbi.nlm.nih.gov/books/NBK1285

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28BSCL2%5BTIAB%5D%29+OR+%28%28seipin%5BTIAB%5D%29+OR+%28SPG17%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- BSCL2 GENE
  http://omim.org/entry/606158

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=BSCL2%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=15832
- Inherited Peripheral Neuropathies Mutation Database
  http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=31
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/26580
- UniProt
  http://www.uniprot.org/uniprot/Q96G97

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